## REMARKS

The pending claims, claims 1, 3-8, 11-20, 27, 29, and 41-53, were rejected. Claims 9-10, 21-26, 28, and 30-40 are canceled as being drawn to a non-elected invention. Claim 1 is amended to limit the claim to measuring the amount of the antibody only. Support may be found throughout the specification. No statutory new matter has been added. Therefore, the Applicants respectfully request that the amendment be entered.

### Rejection under 35 U.S.C. 112, first paragraph

The Examiner rejected claims 1-8 under 35 U.S.C. 112, first paragraph, as the Examiner deemed that an immunoassay for detecting leishmaniasis in a subject by detecting or measuring an antibody *fragment* bound to the soluble antigen is not enabled.

In order to further prosecution, Applicants have amended claim 1 by deleting the phrase "or fragment thereof". Applicants maintain their position set forth in the previous response and reserve the right to pursue the subject matter in a continuation application. Since the claims as amended do not encompass fragments of antibodies, the rejection under 35 U.S.C. 112, first paragraph, may properly be withdrawn.

### Objection to the Specification

As claim 1 no longer recites "fragments", the objection to the specification may properly be withdrawn.

### Rejection under 35 U.S.C. 102(b)

The Examiner rejected claims 1, 3-5, 7, 8, and 41-44 as being anticipated by Martin *et al.* Specifically, the Examiner stated that "[i]t is the Examiner's position that Martin *et al.* used the protein free medium XOM ... the medium is available to the public and it works although the ingredients are not disclosed". The Examiner pointed out that Applicants had not provided any probative evidentiary support that protein free medium XOM is not available to the general public.

Applicants respectfully assert that the present invention as claimed is not anticipated by Martin *et al.* as Martin *et al.* is a non-enabling disclosure. Specifically, as evidenced by (1) the Declaration of Dr. Alan Magill (expert in the field of tropical medicine and diagnostics), (2) the Declaration of Suzannah K. Sundby (Applicants' Attorney), and (3) the letter of 15 April 2002, from GIBCO/Invitrogen, the protein free medium XOM is not available to the general public and the ingredients of XOM were not taught or disclosed prior to the present application.

*Declaration of Dr. Alan Magill*

- **THE DECLARATION OF DR. ALAN MAGILL PROVIDES THAT MARTIN *ET AL.* IS A NON-ENABLING DISCLOSURE.**

The Declaration of Dr. Magill provides that no one of (ordinary or expert) skill in the art is able to practice the present invention as claimed or the assay of Martin *et al.* without having access to a protein free medium, such as XOM, or knowledge of the ingredients in XOM. The Declaration and attached curriculum vitae of Dr. Magill sets forth Dr. Magill's expertise in the field of tropical medicine, diagnostics, and molecular and cellular biology and recombinant DNA techniques. In particular, Dr. Magill has extensive experience with Leishmaniasis diagnostics and vaccines.

As provided in the Declaration, Dr. Magill attests to the fact that:

(1) The use of a protein free medium comprising an oncotic agent, such as XOM is a necessary component of the present invention as claimed;

(2) No one can practice the present invention without having access to a protein free medium comprising an oncotic agent or knowledge of the ingredients in XOM;

(3) A person of ordinary skill in the art would not be able to practice the assay method of the present invention solely by reading Martin *et al.* because (a) until the disclosure of the ingredients of XOM, no one has been able to make a protein free medium in which cells or organisms are viable or may be cultured, and (b) no one realized that the prior art protein free media did not work because no one realized the necessity and criticality of the presence of an oncotic agent to provide a suitable oncotic pressure for cell viability;

(4) Not even Dr. Magill, himself, an expert in the field, would be able to practice the assay method of the present invention without knowledge of the XOM ingredients or access to XOM itself; and

(5) It is Dr. Magill's understanding that no one may obtain XOM or its ingredients from GIBCO/Invitrogen without the authorization or approval from an employee of the United States Army Medical Research and Materiel Command (USAMRMC) or the Walter Reed Army Institute of Research (WRAIR) who has obtained XOM from GIBCO/Invitrogen previously.

Clearly, the Declaration of Dr. Magill sets forth the fact that Martin *et al.* is a non-enabling disclosure as one of ordinary or even expert skill in the art would not be able to practice the present invention as claimed, since Martin *et al.* does not teach or disclose how to make and use the required protein free medium, XOM, and neither XOM nor a similar suitable protein free medium are known in the art, available to the general public, or both.

Applicants note that the Examiner seemed to imply that arguments based on the ingredients of the protein free medium are irrelevant to whether Martin *et al.* anticipates the present invention since the claims of the present invention are directed to an immunoassay and not the composition of the medium. Applicants respectfully submit that the protein free medium is a necessary component of the immunoassays as claimed. Specifically, the immunoassays and also the diagnostic devices and kits of the present invention require that the soluble antigen is prepared by culturing the *Leishmania* parasites in a protein-free medium comprising an oncotic agent. This is a necessary claim limitation that may not be ignored as irrelevant.

As explained in the previous response, the soluble antigens used in the assays are defined as those obtained by culturing the *Leishmania* parasites in protein free medium. In order to culture cells or organisms in protein free medium, the protein free medium must have an oncotic agent that balances the oncotic pressure such that the cells or organisms are viable in the protein free medium. Until the present invention, protein free medium having an oncotic agent was not in the prior art. Thus, the protein free medium comprising an oncotic agent is a critical and necessary component of the present invention, and the ingredients, *i.e.* the oncotic agent, are highly relevant to whether the disclosure of Martin *et al.* is enabled. This fact is supported by the Declaration of Dr. Magill, wherein Dr. Magill declares that no one can practice the present

invention as claimed without having a protein free medium comprising an oncotic agent, such as XOM, or knowledge of the ingredients of XOM.

*Letter from GIBCO/Invitrogen*

- **THE LETTER FROM GIBCO/INVITROGEN PROVIDES EVIDENTIARY SUPPORT THAT NEITHER XOM NOR ITS INGREDIENTS ARE AVAILABLE TO THE GENERAL PUBLIC.**

The letter from GIBCO/Invitrogen outlines the company's policy on custom orders and provides evidence that XOM is not available to the general public. Specifically, the letter provides that:

(1) GIBCO/Invitrogen's policy on custom orders mandates that no third party may obtain the custom order or its ingredients without the approval of one who has previously obtained the product;

(2) XOM is a custom order for WRAIR;

(3) Only the Division of Communicable Diseases and Immunology of the Walter Reed Army Institute of Research (CD&I/WRAIR) have purchased XOM;

(4) XOM was not provided to anyone who did not have authorization through Colonel Samuel K. Martin, Ph.D., one of the inventors of the present invention, of CD&I/WRAIR;

(4) GIBCO/Invitrogen has not and will not provide XOM or its ingredients to third parties who do not have approval by a person who is approved to obtain XOM or have not previously ordered XOM;

(5) There was one unidentified person who attempted to order XOM without approval, and the unidentified person was not given XOM or its ingredients by GIBCO/Invitrogen;

(6) There are no other third parties who have tried to obtain XOM to date; and

(7) GIBCO/Invitrogen will not provide XOM or its ingredients to third parties who do not have approval by one who has previously obtained XOM.

Clearly, the letter by GIBCO/Invitrogen provides evidentiary support that XOM and its ingredients have not been available to the general public.

*Declaration of Suzannah K. Sundby*

- **THE DECLARATION OF SUZANNAH K. SUNDBY PROVIDES EVIDENTIARY SUPPORT THAT THE GENERAL PUBLIC CANNOT OBTAIN XOM OR ITS INGREDIENTS FROM GIBCO/INVITROGEN WITHOUT THE PRODUCT IDENTIFICATION NUMBER AND APPROVAL BY ONE WHO HAS PREVIOUSLY OBTAINED XOM.**

The Declaration of the Applicant's Attorney, Suzannah K. Sundby, provides that on 21 February 2002, she was the unidentified person who tried to order XOM without the product identification number and without approval and that she was not able to obtain XOM or its ingredients. Thus, the Declaration by Attorney Sundby provides that as a member of the general public, she was unable to obtain XOM from GIBCO/Invitrogen.

Therefore, in light of the Declaration of Dr. Magill, the letter from GIBCO/Invitrogen, and the Declaration of Attorney Sundby, Applicants respectfully submit that:

(1) The protein free medium comprising an oncotic agent according to the present invention is a necessary and critical component of the present invention as claimed, and therefore, the ingredients of the protein free medium are highly relevant to whether Martin *et al.* is an enabling disclosure;

(2) Martin *et al.* is not an enabling disclosure as Martin *et al.* does not disclose that the protein free medium comprises an oncotic agent; and

(3) XOM, its ingredients, and suitable protein free medium that may be used according to the present invention have not been available to the general public.

Although Martin *et al.* do disclose an assay which uses the soluble antigens obtained from culturing promastigotes in protein free medium, Martin *et al.* is a non-enabling reference as Martin *et al.* does not disclose that the protein free medium comprises an oncotic agent. The presence of the oncotic agent is a necessary and critical part of the invention. Martin *et al.* does not disclose the presence of the oncotic agent, and neither XOM nor its ingredients were available to the general public. As provided in the Declaration of Dr. Magill, one of skill in the art would not be able to reproduce the experiments of Martin *et al.* without have access to XOM or knowledge of the ingredients of XOM. Therefore, Martin *et al.* is a non-enabling reference and as such, Martin *et al.* cannot be used as prior art against the present invention.

In summary, Martin *et al.* is a non-enabling disclosure as neither XOM nor its ingredients were disclosed or made available to others and knowledge and use of *a protein free medium*

*comprising an oncotic agent*, such as xylose, is necessary in order to practice the present invention. Since Martin *et al.* is a non-enabling reference, Martin *et al.* may not be used to anticipate the present invention as claimed. Because the prior art does not teach or disclose immunoassays, diagnostic devices, or kits that require the use of a protein free medium comprising an oncotic agent, the present invention as claimed is not anticipated. Therefore, the rejection under 35 U.S.C. 102(b) may be properly withdrawn.

**Rejection under 35 U.S.C. 103(a)**

The Examiner rejected the claims under 35 U.S.C. 103(a) as being obvious over Martin *et al.* in view of Wirtz *et al.* and WO 99/56755.

Applicants respectfully submit that the Declaration of Dr. Magill, the letter from GIBCO/Invitrogen, and the Declaration of Attorney Sundby clearly provide evidentiary support that Martin *et al.* does not teach or suggest the use of a protein free medium comprising an oncotic agent and that protein free medium comprising an oncotic agent is not in the prior art. Thus, Applicants respectfully assert that a *prima facie* case of obviousness has not been established. Specifically, the invention as a whole was not taught, disclosed, or suggested by the prior art references. In particular, the use of an oncotic agent in order to practice the invention is not taught, disclosed or suggested anywhere in Martin *et al.*, Wirtz *et al.*, WO 99/56755, or any other reference in the prior art.

The prior art immunoassays have suffered from problems relating to the inability to obtain a pure antigen solely from a given organism. The inability to obtain a pure antigen is due to the fact that an oncotic agent must be present in the media used to culture the organism, and, prior to the present invention, no one in the art understood this to be true. All that was known was that when a completely protein free medium was used, the organisms died. Thus, those skilled in the art always added a protein such as albumin. However, the proteins that are added may contaminate the antigen secreted into the medium. Additionally, the proteins added may be metabolized. When antibodies prepared against such antigenic preparations are used, the antibodies have undesired reactivity against the added proteins and metabolites thereof. Thus, nowhere in the prior art is the use of a soluble antigen obtained from using a protein free medium

comprising an oncotic agent taught, disclosed or suggested for using in an immunoassay with a reasonable expectation of success by one of ordinary skill in the art.

As none of the disclosures of the cited references, alone or in combination, teach, disclose, or suggest each and every limitation of the invention as claimed, the rejection under 35 U.S.C. 103(a) may be properly withdrawn.

**Request for an Interview**

Should there by any remaining issues after entry of the amendment and consideration of the remarks herein, Applicants respectfully request either an in-person interview or a telephonic interview with the Examiner.

**Extension of Time**

A Petition for an Extension of Time for one (1) month under 37 C.F.R 1.136 and the appropriate fee are submitted herewith to extend the time for responding to the Official Action to 18 April 2002.

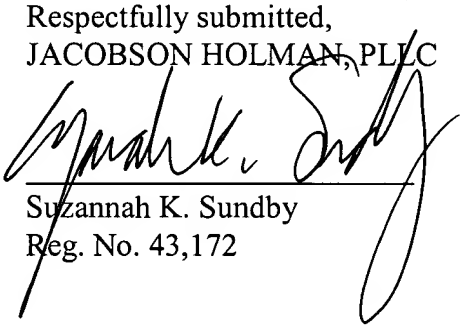
## CONCLUSION

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

It is not believed that extensions of time are required, beyond those that may otherwise be provided for in accompanying documents. However, in the event that additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. §1.136(a), and any fees required therefor are hereby authorized to be charged to our Deposit Account No. **210-380**, referencing Attorney Docket No. **P66748US1 (WRAIR 98-41X).**

Attached hereto is a marked-up version of the changes made by the present amendment entitled "**Version with Markings to Show Changes Made**."

Respectfully submitted,
JACOBSON HOLMAN, PLLC



Suzannah K. Sundby
Reg. No. 43,172

Date: 18 April 2002
400 Seventh Street, N.W.
Washington, DC 20004-2201
(202) 662-8497